LARGE-SCALE SCREENING FOR METABOLIC DEFECTS

Recent progress in biochemical genetics has revealed the existence of many detectable biochemical errors which may lead to serious disease in infants, children, and adults. In addition to phenylketonuria, diseases like galactosemia, maple syrup urine disease, and a variety of others can be detected. The possibility of treating these diseases makes it mandatory to sponsor programs in which the best ways of screening and of treating these diseases can be elucidated. The problems of treatment in each of these diseases are different. In galactosemia, a relatively simple diet causes complete prevention of the disease. In phenylketonuria, a complicated diet initiated sufficiently early in life probably prevents mental retardation, but there is controversy whether treated children are entirely normal. In maple syrup urine disease where the outcome in the absence of treatment is fatal, dietary treatment is extremely complex; and the results are unpredictable and often poor. Work in biochemical genetics has shown that it is likely that in each of these conditions considerable heterogeneity can be found. It is possible, therefore, that conditions showing up as "disease" on initial screening turn out to be innocuous. Particular attention will have to be devoted to the separation of these entities from real disease causing biochemical errors.

The question has been raised whether the cost of extensive screening programs justifies detection of very rare diseases. It seems likely that the phenylketonuria programs have uncovered enough cases of the disease for treatment to have justified their continued existence. Furthermore, the availability of autoanalyzers may make the addition of additional tests of several individually rare diseases possible without much additional cost. Although laws for phenylketonuria screening have been passed in most states of the United States, there is no agreement whether this kind of activity might be better done without passing laws at this time. The complexities of some of these programs also raise the question whether enough trained personnel is available to ensure a high scientific standard and a practicable program all over the country. An initial recommendation for study might be careful evaluation of the phenylketonuria program in the United States. This should include a survey of the way in which current practices for screening are implemented, the effectiveness of the organization of the program in different states, management techniques for treatment with special attention to the differentiation of cases likely to lead to mental retardation from those who are not, and cost effectiveness of the screening programs as compared to other investments in metabolic disease. Consultation should be sought from various committees of the pediatric societies and the World Health Organization who have interested themselves deeply in this matter.

The committee also might pay attention to the feasibility and advisability of screening for more common biochemical errors and other genetic traits which potentially lead to disease. An example of this sort are various hyperlipoproteinemias, some of which are associated with early atherosclerosis. Preventive treatment using drug therapy appears promising and studies testing several agents are under way. Attention also might be paid to the feasibility of storing biologic specimens for later testing of either newly discovered diseases or for conditions where the availability of a newborn specimen would be helpful. It has been pointed out that the placenta is a very rich source of fetal tissue that usually is discarded. The possibility of saving placentae for study of various traits might be considered. Collaboration with an official body of obstetrician/gynecologists would need to be sought for implementation of such a scheme.